
ASTHMA

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PAED DEPTMNT.

Outline

- Overview of asthma
 - Epidemiology of Asthma
 - Risk factors and etiology
 - Clinical Features
 - Diagnosis
 - Overview of asthma management
 - Asthma exacerbations
 - Diagnosis of asthma exacerbation
 - Triggers of asthma exacerbation
 - Management of asthma exacerbations
 - References
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Definition

- **Asthma:** a respiratory disease that is characterized by chronic airway inflammation and manifests with variable respiratory symptoms and expiratory airflow limitation.
 - It is defined by the history of respiratory symptoms, such as wheeze, shortness of breath, chest tightness, and cough, that vary over time and intensity, together with variable expiratory airflow limitation(GINA 2023).
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Epidemiology

✂ **Most common chronic disease of childhood.**

✂ Onset:

80% of cases present **before age 6.**

Children (<14 years):

- Boys > Girls (ratio $\approx$ 2:1)
- Global prevalence in children:
- **5-10%** in most countries.
- In Uganda , 10-20%

Risk factors and etiology

TABLE 281-1 Risk Factors and Triggers Involved in Asthma

ENDOGENOUS FACTORS	ENVIRONMENTAL FACTORS
Genetic predisposition Atopy Airway hyperresponsiveness Gender Ethnicity Obesity Early viral infections	Indoor allergens Outdoor allergens Occupational sensitizers Passive smoking Respiratory infections Air pollution (diesel particulates, nitrogen oxides) Diet Dampness and mold exposure Acetaminophen (paracetamol)
Triggers	
Allergens Upper respiratory tract viral infections Exercise and hyperventilation Cold air Sulfur dioxide and irritant gases Drugs (β -blockers, aspirin) Stress Irritants (household sprays, paint fumes)	

ATOPY

- The relationship between atopy (the propensity to produce IgE) and asthma is well established and in many individuals.
- There is a clear relationship between sensitization and allergen exposure, as demonstrated by skin-prick reactivity or elevated serum-specific IgE.
- Common examples of allergens includes house dust mites, pets such as cats, dogs, cockroaches, and fungus.
- Inhalation of these allergens into the airway is followed by an early and late-phase bronchoconstrictor response.

Genetic predisposition

- There is a high degree of concordance among identical twins, and also familial association of asthma.

NSAIDS/Aspirin-sensitive asthma

- In cases of aspirin-sensitive asthma, the ingestion of salicylates results in inhibition of the **cyclo-oxygenase enzymes**, preferentially shunting the metabolism of arachidonic acid through the **lipxygenase pathway** with resultant production of the asthmogenic cysteinyl leukotrienes.

Exercise-hyperventilation

- In exercise-induced asthma, hyperventilation results in water loss from the pericellular lining fluid of the respiratory mucosa, which, in turn, triggers mediator release.
- Heat loss from the respiratory mucosa may also be important.

Infections

- ~~□ Viral infections are common as triggers of asthma exacerbations, it is uncertain whether they play a role in etiology.~~

❖ **Obesity:**

especially women have increased production of pro-inflammatory adipokines (TNF- α and IL-6) and anti inflammatory adipokines from fat cells.

❖ **Allergens:**

trigger asthma response but are not implicated in allergic sensitization; rigorous avoidance of allergens has not reduced the risk to develop asthma.

❖ **Acetaminophen(oxidative stress):**

Metabolites of acetaminophen depletes glutathione levels in the respiratory tract and thus leads to vulnerability to oxidative stress.

❖ **Food and diet:** Diet with low antioxidants e.g. Vitamin A and C, Mg, Selenium, Omega 3, Omega 6, high sodium, Vitamin D deficiency can cause asthma.

❖ **Hormones** Thyrotoxicosis and hypothyroidism can both worsen asthma,

Physical Factors

- Cold air and hyperventilation may trigger asthma through the same mechanisms as exercise.
- Some asthmatics become worse when exposed to strong smells or perfumes, but the mechanism of this response is uncertain.

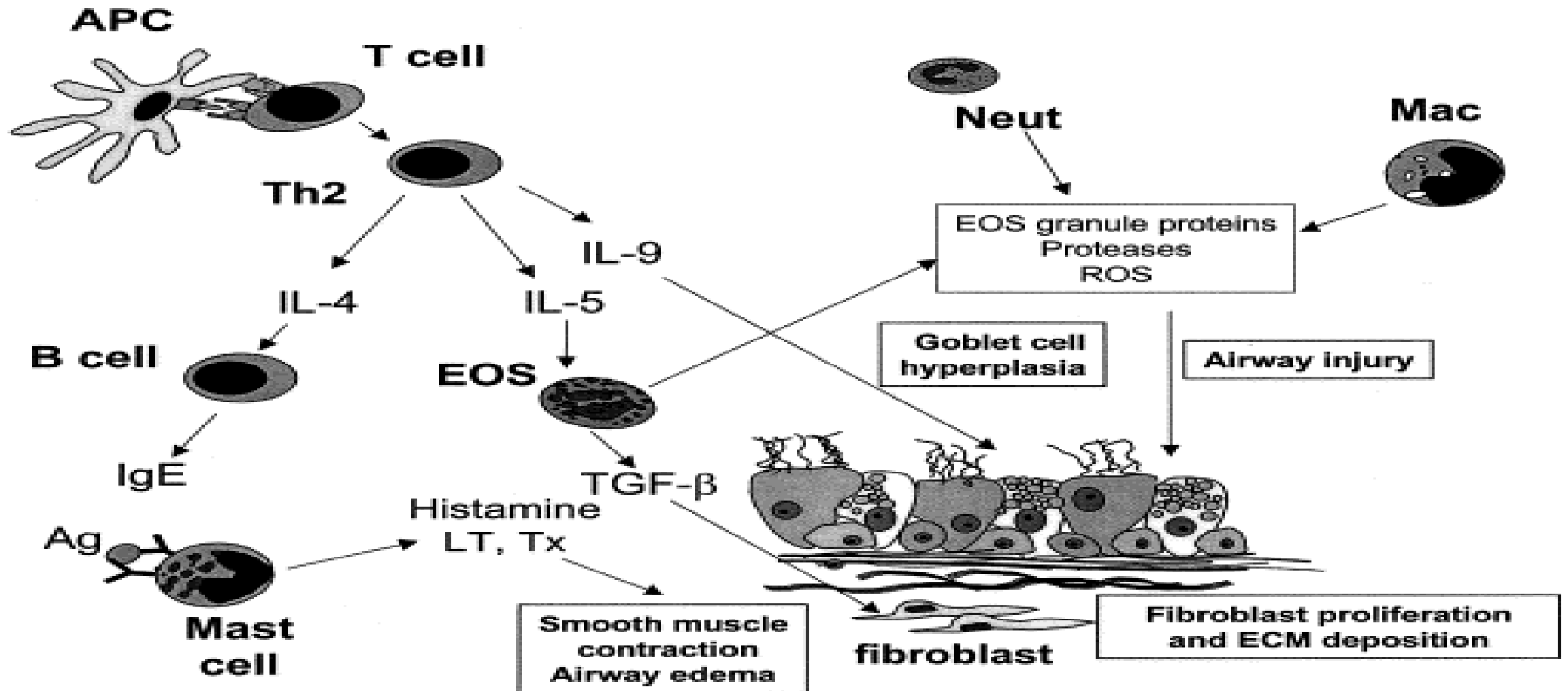
Other factors

- Low maternal age
 - Duration of breast feeding
 - Prematurity
 - Low birth weight
 - Inactivity
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Pathophysiology

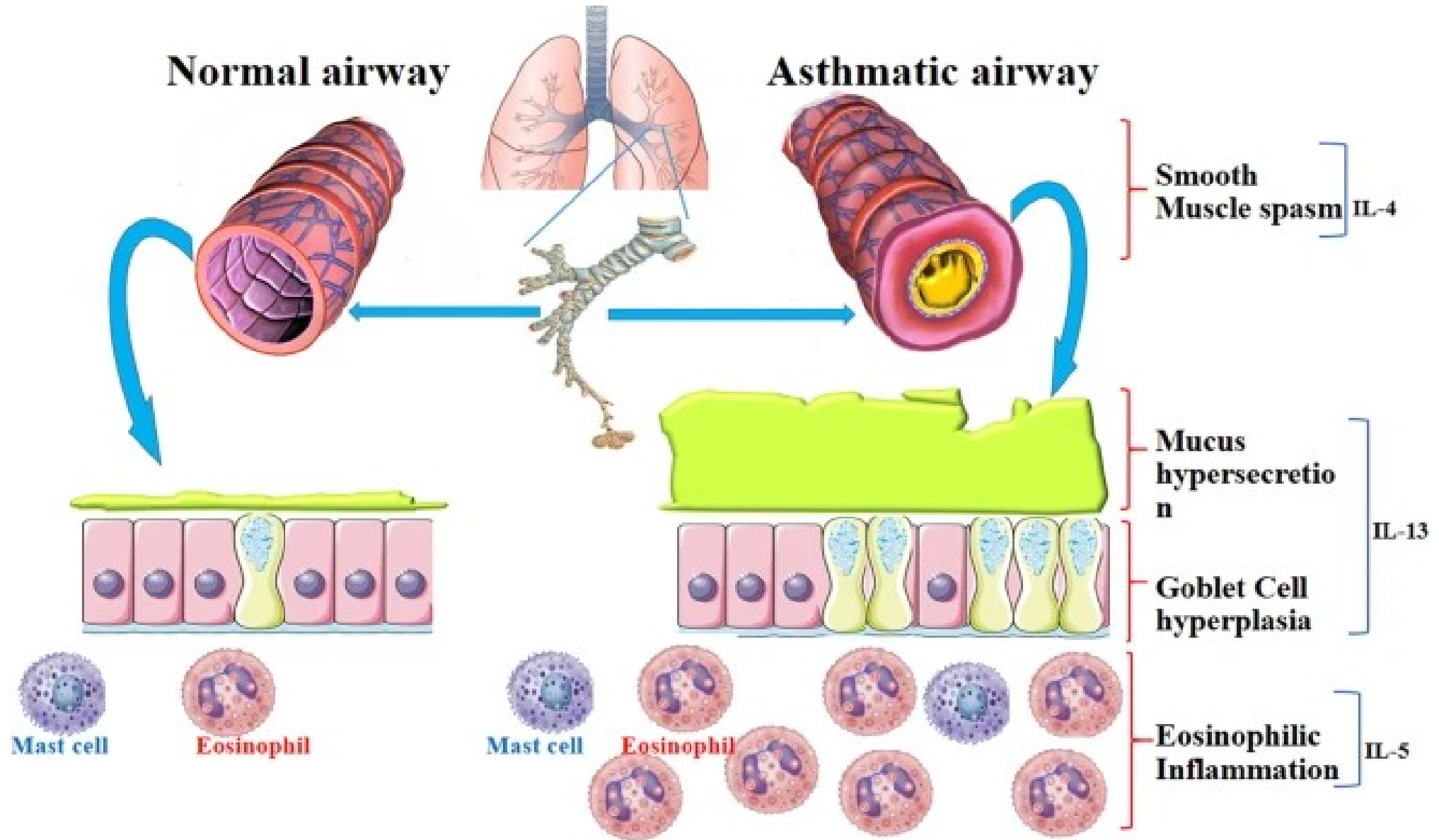
- The allergic response starts with antigen (Ag) sensitization, in which an antigen-presenting cell (APC) digests Ag.
- It then presents it to a naïve T cell which subsequently differentiate into a Th2 cell.
- The Th2 cell is then capable of generating various cytokines, including: IL-4, IL 5 AND IL 9 & 13.
- IL 4 promotes IgE synthesis via a B cell;
- IL-5, which promotes eosinophil (EOS) maturation and activation;
- IL-9 and IL-13, which promote goblet cell hyperplasia and mucous secretion.
- the mast cell are triggered by Ag-IgE cross-linking to release histamine, leukotrienes (LT), and thromboxane's (Tx) that cause smooth muscle contraction and airway edema.
- Eosinophil-derived granule proteins lead to airway injury.
- Airway injury can also be caused by proteases and reactive oxygen species (ROS) released by EOS, neutrophils (Neut), and macrophages (Mac).
- Profibrotic cytokines such as transforming growth factor β (TGF- β) can promote fibroblast proliferation, generation and deposition of extracellular matrix (ECM) proteins promoting subepithelial fibrosis and airway remodeling.

Cont.....



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- With increasing severity and chronicity of the disease, remodeling of the airway may occur, leading to fibrosis of the airway wall, fixed narrowing of the airway and a reduced response to bronchodilator medication.



Phenotypes of Asthma

- The pathology of asthma is remarkably uniform in different phenotypes of asthma, including;
 - ▣ **Atopic (extrinsic),**
 - Asthma triggered by exposure to specific allergens in individuals who are genetically predisposed to develop an IgE-mediated hypersensitivity reaction. Often starts in childhood or adolescence. Positive skin prick tests to specific allergens
 - ▣ **Non-atopic (intrinsic),**
 - Negative skin prick test, normal serum IgE, it is mostly adult onset. e.g.: nasal polyps, and aspirin sensitive.
 - May be severe and persistent.

Clinical features of Asthma

- Asthma may develop at any age. While it is a common in childhood.
- Some patients will report all four of the classic symptoms of asthma, while others may report only one or two:
 - Wheeze (high-pitched whistling sound, usually upon exhalation).
 - Cough (often worse at night).
 - Shortness of breath or difficulty breathing.

Physical Examination

- **Vital sign.**

- **:increased respiratory rates**
- creased heart rate, cardiac output, and blood pressure.

- ❖ **Pulsus paradoxus:**

1. Decreased blood pressure during inspiration.
2. Increased blood pressure during expiration.

- Wheeze apart, there is often very little to find on examination.
- Use of accessory muscles for both inspiration and expiration
- Cyanosis
- Cough and sputum production

Chest examination

- Hyper resonant percussion
 - Diminished breath sounds
 - **Wheezing** and rhonchi
 - Expiratory PHASE prolongation
 - Decreased tactile and vocal fremitus
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Diagnosis

- Detailed history taking and physical examination
- Lung function tests
- Chest x-ray/chest CT scan
- ABGs and
- CBCs
- Pulse oximetry
- Allergy skin test
- Serum IgE

History and Physical Examination

❖ **History -**

- Symptoms **e.g.** exacerbate at night or early morning, exercise induced symptoms, home, work or recreational exposure.

➤ **P/E -**

- **Wheezing, tachypnea, tachycardia, use of accessory muscles.**
- May be **normal** P/E in b/n exacerbations.
- **Silent** chest (in Severe Asthma).

➤ **Simple spirometry:**

- ✓ Essential to initial evaluation.
- ✓ Helps assess severity of airflow obstruction/response to treatment.

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- Aids in differential diagnosis.
 - ▣ Obstructive versus restrictive airway disease.
 - ▣ Reversibility of airflow obstruction.
- Obstructive pattern: confirms airflow limitation with a reduced FEV1, FEV1/FVC ratio.
- Restrictive pattern: reduced FVC with a normal FEV1/FVC ratio.

Pulmonary Function Tests:

>5yrs

- **PEFR, FEV1, FEV1/FVC ratio** – All are reduced in Asthma.

Peak Flow Monitoring

- Peak expiratory flow (PEF) measurement is common in the ED because it is inexpensive and portable.
- Serial measurements document response to therapy and, along with other parameters, are helpful in determining whether to admit the patient to the hospital or discharge from the ED.
- A limitation of PEF is that it is dependent on effort by the patient.
- FEV_1 is also effort dependent but less than PEF.
- FEV_1 is not often used in the ED except in research settings.

Arterial Blood Gas

- **Arterial Blood Gas (ABG) Measurement** provides important information in acute asthma.
- This test may reveal dangerous levels of hypoxemia or hypercapnia secondary to hypoventilation and, hence, respiratory acidosis.
- However, the typical finding in the early stages of an acute episode is respiratory alkalosis.
- Because of the accuracy and utility of pulse oximetry, only patients whose oxygenation is not restored to over 90% with oxygen therapy require an ABG.

Chest Radiography

- ❖ In most patients with asthma, chest radiography findings are normal or may indicate hyperinflation.
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Chest CT Scanning

- High-resolution CT (HRCT) is a second-line investigation.
 - It is useful in patients with chronic or recurring symptoms and in those with possible complications such as allergic bronchopulmonary aspergillosis and bronchiectasis.
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Differential Diagnosis

- Tumor of Upper airway.
- laryngeal edema.
- Endobronchial obstruction with a foreign body.
- Left ventricular failure.
- Vocal cord dysfunction(hysterical conversion syndrome).
- Eosinophilic pneumonias.
- Chronic obstructive pulmonary disease (COPD).

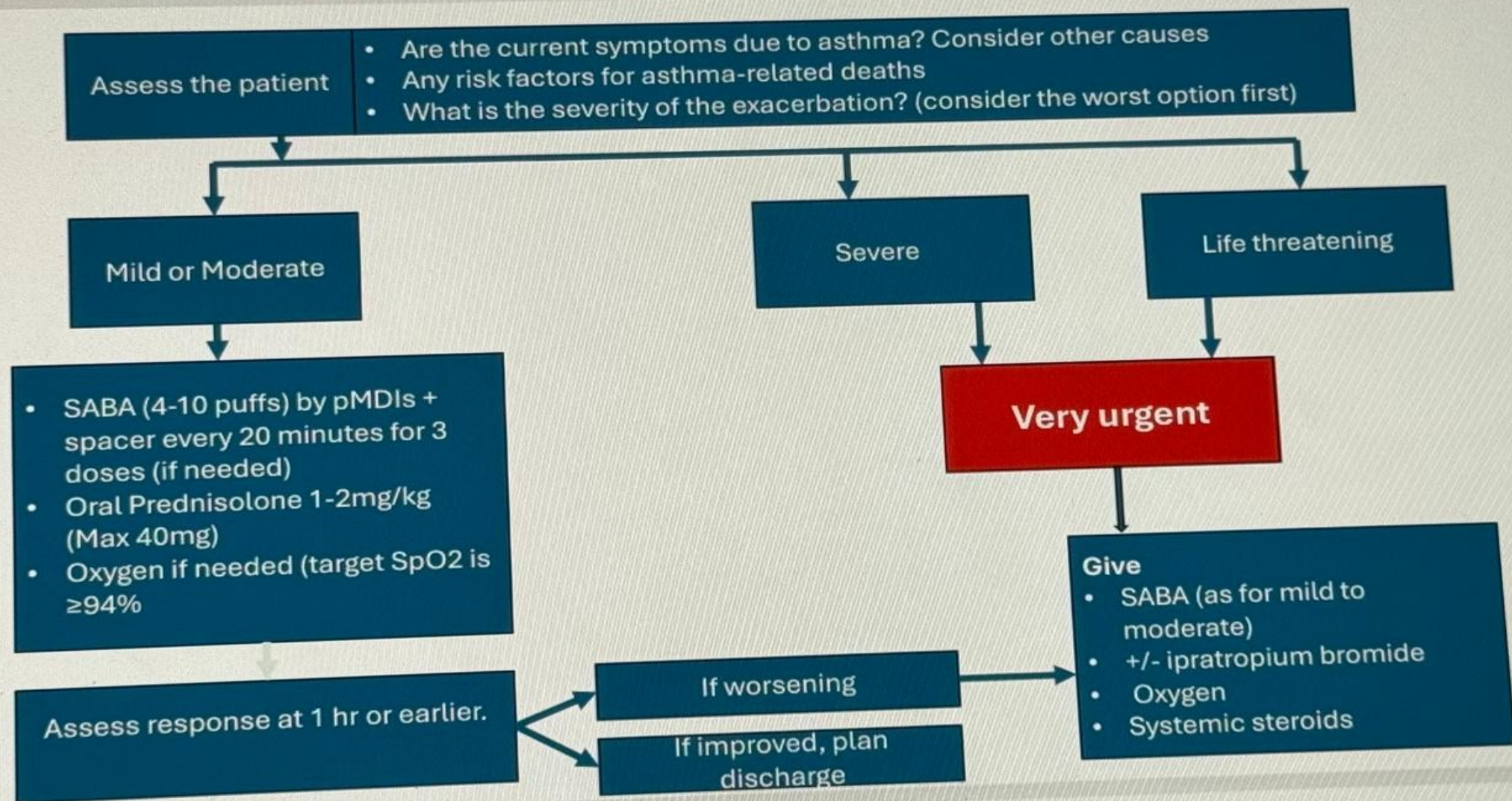
Management of Asthma

Goals:

- To relieve the airflow obstruction and hypoxaemia (if present)
 - Address the underlying inflammation
 - Prevent relapse
 - Note:
 - Do not forget complications and comorbidities if present.
 - Make sure the triggers are also managed
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❖ **Avoidance of aggravating factors:**

- particularly important occupational asthma.
 - relevant to atopic patients where removing or reducing exposure to relevant antigens, e.g. a pet animal, may effect improvement.
 - House dust mite exposure may be minimized by replacing carpets with floorboards and using mite impermeable bedding.
 - Measures to reduce fungal exposure and eliminate cockroaches.
 - Medications known to precipitate or aggravate asthma should be avoided.
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- Salbutamol Via MDI and spacer

<6 years 4 puffs per dose

6-12 years 4-6 puffs per dose

>12years 6-10 puffs per dose

- Ipratropium bromide

< 4 years 125mcg

4-11 years 250mcg

≥12 years 500mcg

- Oral Prednisone or prednisolone

1-2mg/kg/day, for 3-5 days,

max 20mg less than 2yrs

max 30mg 3-5 yrs

max 40mg for older children

STARTING ASTHMA TREATMENT

For the best outcomes, **ICS-containing treatment should be initiated** as soon as possible after the diagnosis of asthma is made, because:

- Patients with even mild asthma can have severe exacerbations
- Low dose ICS markedly reduces asthma hospitalizations and death
- Low dose ICS is very effective in preventing severe exacerbations, reducing symptoms, improving lung function, and preventing exercise-induced bronchoconstriction, even in patients with mild asthma
- Early treatment with low dose ICS is associated with better lung function than if symptoms have been present for more than 2–4 years
- Patients not taking ICS who experience a severe exacerbation have lower long-term lung function than those who have started ICS
- In occupational asthma, early removal from exposure and early treatment increase the probability of recovery

COMBINATION SHORT-ACTING BETA₂-AGONIST PLUS ANTICHOLINERGIC IN ONE DEVICE (SABA/SAMA)

Fenoterol/ipratropium	SMI				6-8 hours
Salbutamol/ipratropium	SMI, MDI				6-8 hours

COMBINATION LONG-ACTING BETA₂-AGONIST PLUS ANTICHOLINERGIC IN ONE DEVICE (LABA/LAMA)

Formoterol/acclidinium	DPI				12 hours
Formoterol/glycopyrronium	MDI				12 hours
Indacaterol/glycopyrronium	DPI				12-24 hours
Vilanterol/umeclidinium	DPI				24 hours
Olodaterol/tiotropium	SMI				24 hours

METHYLYXANTHINES

Aminophylline			solution	✓	Variable, up to 24 hours
Theophylline (SR)			pill	✓	Variable, up to 24 hours

COMBINATION OF LONG-ACTING BETA₂-AGONIST PLUS CORTICOSTEROID IN ONE DEVICE (LABA/ICS)

Formoterol/beclometasone	MDI, DPI				12 hours
Formoterol/budesonide	MDI, DPI				12 hours
Formoterol/mometasone	MDI				12 hours
Salmeterol/fluticasone propionate	MDI, DPI				12 hours
Vilanterol/fluticasone furoate	DPI				24 hours

TRIPLE COMBINATION IN ONE DEVICE (LABA/LAMA/ICS)

Fluticasone/umeclidinium/vilanterol	DPI				24 hours
Beclometasone/formoterol/glycopyrronium	MDI				12 hours



ACUTE ASTHMA EXACERBATION

ACUTE ASTHMA EXACERBATION

■ **Definition of asthma exacerbation:**

- Exacerbation of asthma characterized by a progressive increase in symptoms of shortness of breathing, cough, wheezing, or chest tightness and a progressive decrease in lung function(GINA 2023).
- The term exacerbation is commonly used in scientific and clinical literature, some hospital-based studies more often refer to acute severe asthma. And the term attack used by many patients and healthcare providers.
- Exacerbations may occur in patients with a pre-existing diagnosis of asthma or occasionally as the first presentation of asthma.

❖ **What triggers asthma exacerbation**

- Exacerbations usually occur in response to an external agent (eg viral URTI, pollen, or pollution) or poor adherence to ICS-containing medications.

Common exacerbation triggers include

- Viral respiratory infections (rhinovirus, influenza, adenovirus, RSV, pertussis).
- Allergens (e.g.; grass pollen, soybean dust, and fungal spores).
- Food allergy
- Outdoor air pollution
- Seasonal change and or returning to school in fall (autumn)
- Poor adherence to ICS

Diagnosis of exacerbation

- Peak expiratory measurement
- Pulse oximetry
- ABG
- Chest radiograph:
 - Chest radiographs are generally unrevealing in acute asthma attacks and are not routinely required in the urgent care setting.
 - However, a chest radiograph should be obtained when a complicating cardiopulmonary process is suspected (eg, temperature $>38.3^{\circ}\text{C}$, unexplained chest pain, leukocytosis, or hypoxemia), when a patient requires hospitalization, and when the diagnosis is uncertain(GINA 2023).



Moderate asthma	Increasing symptoms PEF >50–75% best or predicted No features of acute severe asthma	
Acute severe asthma	Any one of: - PEF 33–50% best or predicted - respiratory rate $\geq 25/\text{min}$ - heart rate $\geq 110/\text{min}$ - inability to complete sentences in one breath	
Life-threatening asthma	Any one of the following in a patient with severe asthma:	
	Clinical signs	Measurements
	Altered conscious level	PEF <33% best or predicted
	Exhaustion	SpO ₂ < 92%
	Arrhythmia	PaO ₂ < 8 kPa
	Hypotension	'normal' PaCO ₂ (4.6–6.0 kPa)
	Cyanosis	
	Silent chest	
	Poor respiratory effort	
Near-fatal asthma	Raised PaCO ₂ and/or requiring mechanical ventilation with raised inflation pressures ⁵⁰⁴⁻⁵⁰⁷	

PaO₂: partial arterial pressure of oxygen

kPa: kiloPascals

PaCO₂: partial arterial pressure of carbon dioxide

Management of asthma exacerbation in Emergency department

- The primary goals of therapy for acute severe asthma are the rapid reversal of airflow limitation and the correction.
- Airflow limitation is most rapidly alleviated by the combination of repeated administration of inhaled bronchodilators and early institution of systemic glucocorticoids.

Emergency Department Management

- Initial assessment (A, B, C).
- **Oxygen**
 - Supplemental oxygen should be administered by nasal cannulae or mask to all patients with hypoxemia [SpO_2] <90%.

■ **Inhaled beta-agonists**

- ❑ Inhaled bronchodilator treatment (SABA), such as salbutamol should be administered frequently in patients present with acute asthma attacks.
- ❑ Use of nebulizers can disseminate aerosols and potentially contribute spread

- Four to six carefully administered inhalations from an MDI with chamber/spacer have generally been found to equal one nebulizer treatment.
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- **Standard nebulization** – Salbutamol 2.5 to 5 mg by nebulization every 20 minutes for three doses, then 2.5 mg to 5 mg every one to four hours as needed.
- Of note, the higher doses are associated with more frequent and severe sympathomimetic side effects and are generally reserved for very severe, refractory attacks.

- **Metered dose inhaler (MDI)** – Salbutamol by MDI with a spacer 4 to 8 puffs every 20 minutes, for the first hour.
- The higher number of puffs is associated with a greater likelihood of tremor and tachycardia.

Inhaled muscarinic antagonists

- In accordance with current guidelines for asthma exacerbations, we recommend addition of inhaled [ipratropium](#), (SAMA) to inhaled SABA for patients who present to the emergency department with a severe exacerbation of asthma
- **Dosing –**
 - The dose of [ipratropium](#) is 500 mcg by nebulization or four to eight puffs by MDI, every 20 minutes for three doses, and then hourly as needed for up to three hours
- **Duration –**
 - We advise stopping inhaled SAMA therapy once the patient is admitted to the hospital, except in patients with refractory asthma who require

Systemic corticosteroids

- Systemic corticosteroids speeds resolution of exacerbation and prevent relapse.
- Systemic corticosteroid should administered with 1h od presentation.
- **Route:**
 - Oral administration is effective as intervenous.
 - Use IV when patient is too dyspneic to swallow or vomiting.
- **Dose:**
 - ✂ Prednisolone **1-2 mg/kg/day (max 40-60 mg)**
 - ✂ IV hydrocortisone **4 mg/kg every 6 h** if unable to take orally
- **Duration:** 3 to 5 days

■ Immediate Management (in ED or hospital)

Step	Medication	Dose
1	Salbutamol(SABA)MDI+spacer	<6years;2-6 puffs >_ 6years;4-10 puffs
2	Ipratropium bromide	Neb 250 µg q20min × 1 hr
3	Systemic corticosteroid	Prednisolone 1-2 mg/kg/day (max 40-50 mg) orally; IV hydrocortisone if unable to take PO
4	Oxygen	Maintain SpO ₂ 94-98%
5	IV therapy (for poor response)IV magnesium sulfate	50 mg/kg over 20 min (max 2 g)

■ Long-Term Control Children 6–11 years

Step	Preferred controller	Reliever
1	Low-dose ICS taken whenever SABA is taken	SABA
2	Daily low-dose ICS	SABA
3	Low-dose ICS-LABA, or medium-dose ICS	SABA
4	Medium-dose ICS-LABA	SABA

For children <5 years

Step	
1	SABA for relief; ICS trial if symptoms frequent.
2	Daily low-dose ICS.
3	Double ICS dose

Other treatments

- **Aminophylline and theophylline:**
 - Should not be used in the management of asthma exacerbation, in the view of their poor efficacy and safety.
 - **Magnesium:**
 - IV magnesium sulfate shouldn't be routinely used in asthma exacerbations.
 - **Antibiotics:**
 - Evidence doesn't support routine use of antibiotics in asthma exacerbation unless there is strong evidence of lung infection(normansell R et al 2018) GINA 2023.
 - **Sedatives** : must be avoided.
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Reviewing response

- Clinical status and oxygen saturation should be assessed frequently.
- Lung function test should be measured after 1h. eg: after first three bronchodilator treatment.
- Patient who deteriorate despite intensive treatment of bronchodilator and corticosteroid treatment should re-evaluated for transfer to ICU.

■ **Key messages**

- ✓ No need for antibiotics unless indicated (evidence of bacterial infection)
 - ✓ No need for a nebulizer except in severe or life threatening exacerbations
 - ✓ Oral corticosteroids should be 1st choice (time of onset of action is the same for IV hydrocortisone)
 - ✓ Always ensure correct inhaler use and train caregiver/patient
 - ✓ Re-assess patient frequently
 - ✓ At discharge start ICS
 - ✓ Follow up plan (within a few days + long term care)
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References

- GINA guidelines 2024
 - Nelson
 - <https://pubmed.ncbi.nlm.nih.gov/30795752/> / Prevalence and factors associated with asthma among adolescents and adults in Uganda: a general population based survey,
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I can't breathe
without you